confluence. The cultivated cells were seeded into a 48-well plate in a density of 2.5 x 10^5 cells/well, and incubated therein for 3 days under the same condition as above. Then, the culture medium was removed through suction.

A dimethylformamide (DMF) solution containing a test compound was dissolved in 0.5 ml of 0.5% BSA/DMEM, and added to the plate, and the cells were incubated for further 24 hours. As the control, the same volume of DMF but not containing the test compound was dissolved in 0.5 ml of 0.5% BSA/DMEM, and added to the plate.

The supernatant was collected from the plate, and stored at -20°C or lower until the measurement of its Aβ content.

(2) Enzyme Immunoassay (EIA) for Aβ

BAN-50 antibody or BNT-77 antibody was used as the primary antibody. To determine the $A\beta_{1-40}$ of each sample, used was BA-27 antibody as the secondary antibody. To determine the $A\beta_{1-42}$ of each sample, used was BC-05 antibody as the secondary antibody.

BAN-50 antibody or BNT-77 antibody as dissolved in 0.1 M carbonic acid buffer (pH 9.6) in a concentration of 15 μg/ml was added to a polyethylene microtiter plate in an amount of 100 μl/well, and kept at 4°C overnight. The surface of the plate was washed three times with PBS, and 200 μl of a blocking solution (25% Block Ace/0.1% sodium azide/PBS) was added to the plate. Under this condition, the plate was kept at 4°C before the addition thereto of the supernatant prepared in (1).

Just before the addition of the supernatant, the surface of the plate was washed three times with PBS, and 50 μl of a buffer for primary reaction (20 mM phosphate buffer, pH 7.0; 400 mM NaCl; 2 mM EDTA; 10% Block Ace; 0.2% BSA; 0.05% sodium azide) was added to

the plate. Next, 100 µl of the supernatant and 100 µl of standard $A\beta_{1-40}$ or $A\beta_{1-42}$ as diluted in the buffer for primary reaction (to have a varying concentration of 1000, 200, 40 or 8 pg/ml) were added to the plate, and then kept overnight at 4° C.

The plate was washed three times with PBS, and 100 µl of an HRP-labeled secondary antibody (BA-27 antibody or BC-05 antibody labeled with HRP, horseradish peroxidase) as dissolved in a buffer for secondary reaction (20 mM phosphate buffer, pH 7.0; 400 mM NaCl; 2 mM EDTA; 1 % BSA) was added thereto. After having been left at room temperature for 6 hours, the plate was washed seven times with PBS, and 100 µl of a coloring reagent (TMB Peroxidase Substrate, trade name, manufactured by Kirkegaard & Perry Lab.) was added thereto. This was left at room temperature for 8 to 10 minutes, and 100 µl of 1 M phosphoric acid solution was added to the plate to stop the reaction. Then, using a plate reader (MTP-32 Microplate Reader, by Corona Co.), the sample on the plate was subjected to colorimetric determination (at 450 nm).

(Results)

Four wells were used for one dose of the test compound.

The effect of the test compound (10 µM) to inhibit the production and/or secretion of $A\beta_{1-40}$ and $A\beta_{1-42}$ was obtained in terms of the percentage (%) relative to the control. The data obtained are shown in Table 1.

[Table 1]

Test Compound (Ex. No.)	Aβ1-40 (%)	Aβ1-42 (%)
Example 12	74	75

The above data verify that compound (I) of the present invention and compound (I') have the effect of inhibiting amyloid-β protein production and/or secretion.

INDUSTRIAL APPLICABILITY

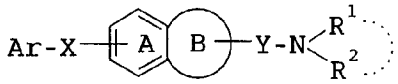
Compound (I) of the present invention has both an excellent inhibitory effect on amyloid-β protein production and/or secretion and an excellent stimulating effect on secreted form of amyloid precursor protein (sAPP) secretion, while having low toxicity, and has excellent mobility into the brain.

Compound (I') also has the inhibitory effect on amyloid-β protein production and/or secretion and stimulating effect on sAPP secretion.

Therefor, compounds (I) and (I') are useful as safe medicines for preventing and/or treating neurodegenerative disorders (e.g., Alzheimer's disease, Down's syndrome, senile dementia, Parkinson's disease, Creutzfeldt-Jacob disease, amyotrophic sclerosis on lateral fasciculus of spinal, diabetic neuropathy, Huntington's disease, multiple sclerosis, etc.), amyloid angiopathy, neurological disorders caused by cerebrovascular disorders (e.g., cerebral infarction, encephalorrhagia, etc.), a head injury or an injury of spinal cord, as well as ameliorating derangements (for example, depression, anxiety, compulsive neurosis, sleep disorders, etc.) caused by neurodegenerative disorders or neurological disorders, especially for neurodegenerative disorders caused by amyloid-β protein (e.g., Alzheimer's disease, Down's syndrome, etc.).

CLAIMS

1. A compound of the formula:



wherein Ar represents an aromatic ring assembly group which may be substituted or a fused aromatic group which may be substituted;

X represents (i) a bond, (ii) -S-, -SO- or $-SO_2-$, (iii) a C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene group, each of which may be substituted by 1 to 3 substituents selected from the group consisting of oxo and C_{1-6} alkyl, (iv) -CO-O- or (v) a group of the formula: $-(CH_2)p-X^1-$, $-(CH_2)p-X^1-(CH_2)q-$, $-(CH_2)r-CO-X^1-$, $-SO_2-NR^8-$ or $-(CH_2)r-SO_2-NR^8-$

wherein X^1 represents O or NR^8,

R^8 represents a hydrogen atom, a hydrocarbon group which may be substituted or an acyl, p represents an integer of 0 to 5, q represents an integer of 1 to 5, p+q is an integer of 1 to 5, and r represents an integer of 1 to 4;

Y represents a divalent C_{1-6} aliphatic hydrocarbon group which may contain an oxygen atom or a sulfur atom and may be substituted;

R^1 and R^2 each represents a hydrogen atom or a lower alkyl which may be substituted, or

R^1 and R^2 form, taken together with the adjacent nitrogen atom, a nitrogen-containing heterocyclic ring which may be substituted;

Ring A represents a benzene ring which may be further substituted apart from the group of the formula: -X-Ar wherein each symbol is as defined above; and

Ring B represents a 4- to 8-membered ring which may be

further substituted apart from the group of the formula: -Y-NR^1R^2 wherein each symbol is as defined above;

provided that, when the fused ring to be formed by Ring A and Ring B is an indole ring, the group of the formula: -X-Ar wherein each symbol is as defined above is substituted on 4-, 6- or 7-position of the indole ring,

or a salt thereof.

2. A compound of claim 1, wherein

Ar is (i) an aromatic ring assembly group which is composed of two or three rings selected from the class consisting of a C_{6-14} aromatic hydrocarbon, a C_{6-14} quinone and a 5- to 14-membered aromatic heterocyclic ring containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms in addition to carbon atoms, which rings are directly bonded to each other via a single bond, and which assembly group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-

carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, or

(ii) a fused bi- or tri-cyclic C_{10-14} aryl or 9- to 14-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy;

R^8 is (a) a hydrogen atom,
(b) a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl being optionally condensed with one benzene ring, C_{6-14} aryl or C_{7-19} aralkyl group which may be substituted by 1 to 5 substituents selected form the group consisting of (1) halogen atoms, (2) C_{1-3} alkylenedioxy, (3) nitro, (4) cyano, (5) optionally halogenated C_{1-6} alkyl, (6) optionally halogenated C_{3-6} cycloalkyl, (7) optionally halogenated C_{1-6} alkoxy, (8) optionally halogenated C_{1-6} alkylthio, (9) hydroxy, (10) amino, (11) mono-C_{1-6} alkylamino, (12) di-C_{1-6} alkylamino, (13) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl, (14) formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido or C_{1-6} alkylsulfonylamino, (15) C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy or nicotinoyloxy, (16) 5- to 7-membered saturated cyclic amino, (17) sulfo, (18) a phenyl or 5- or 6-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, each of which may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy,

nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (19) an aromatic ring assembly group which is composed of two or three rings selected from the class consisting of a C_{6-14} aromatic hydrocarbon, a C_{6-14} quinone and a 5- to 14-membered aromatic heterocyclic ring containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms in addition to carbon atoms, are directly bonded to each other via a single bond, and which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6}

alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, and (20) a fused bi- or tri-cyclic C_{10-14} aryl or 9- to 14-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-

membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, or

(c) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl;

Y is a C_{1-6} alkylene, a C_{2-6} alkenylene, a C_{2-6} alkynylene or a group of the formula: $-(CH_2)m-Y^1-(CH_2)n-$ wherein $-Y^1-$ is -O-, -S-, -SO- or $-SO_2-$,

m is an integer of 0 to 4,

n is an integer of 1 to 5, and

m+n is an integer of 1 to 5;

R^1 and R^2 each is a hydrogen atom or a C_{1-6} alkyl which may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy,

carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy, C_{6-10} aryloxy and C_{6-10} aryl or

R^1 and R^2 form, taken together with the adjacent nitrogen atom, a 3- to 8-membered nitrogen-containing heterocyclic ring having one nitrogen atom and optionally having 1 to 3 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which ring may be substituted by 1 to 5 substituents selected from the group consisting of (1) halogen atoms, (2) C_{1-3} alkylenedioxy, (3) nitro, (4) cyano, (5) optionally halogenated C_{1-6} alkyl, (6) optionally halogenated C_{3-6} cycloalkyl, (7) optionally halogenated C_{1-6} alkoxy, (8) optionally halogenated C_{1-6} alkylthio, (9) hydroxy, (10) amino, (11) mono-C_{1-6} alkylamino, (12) di-C_{1-6} alkylamino, (13) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10}

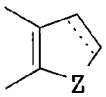
aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl, (14) formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido or C_{1-6} alkylsulfonylamino, (15) C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy or nicotinoyloxy, (16) 5- to 7-membered saturated cyclic amino, (17) sulfo, (18) a phenyl or 5- or 6-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, each of which may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10}

aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (19) an aromatic ring assembly group which is composed of two or three rings selected from the class consisting of a C_{6-14} aromatic hydrocarbon, a C_{6-14} quinone and a 5- to 14-membered aromatic heterocyclic ring containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms in addition to carbon atoms, are directly bonded to each other via a single bond, and which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (20) a fused bi- or tri-cyclic C_{10-14} aryl or 9- to 14-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of

nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (21) an oxo and (22) C_{7-19} aralkyl;

Ring A is a benzene ring which may be further substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{1-6} alkoxy, hydroxy and amino, apart from the group of the formula: -X-Ar wherein each symbol is as defined above; and

Ring B is a 4- to 8-membered ring of the formula:



wherein ---- is a single bond or a double bond, and Z is (i) a bond, (ii) a C_{1-4} alkylene, (iii) a C_{2-4} alkenylene, (iv) $-O-CH_2-$, (v) $-O-CH_2-CH_2-$ or (vi) a group of the formula: $-NR^{8a}-CH_2-$ or $-NR^{8a}-CH_2-CH_2-$ wherein R^{8a} is (a) a hydrogen atom, (b) a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl being optionally condensed with one benzene ring, C_{6-14} aryl or C_{7-19} aralkyl group which may be substituted by 1 to 5 substituents selected form the group consisting of (1) halogen atoms, (2) C_{1-3} alkylenedioxy, (3) nitro, (4) cyano, (5) optionally halogenated C_{1-6} alkyl, (6) optionally halogenated C_{3-6} cycloalkyl, (7) optionally halogenated C_{1-6} alkoxy, (8) optionally halogenated C_{1-6} alkylthio, (9) hydroxy, (10) amino, (11) mono-C_{1-6} alkylamino, (12) di-C_{1-6} alkylamino, (13) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl, (14) formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido or C_{1-6} alkylsulfonylamino, (15) C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy or nicotinoyloxy, (16) 5- to 7-

membered saturated cyclic amino, (17) sulfo, (18) a phenyl or 5- or 6-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, each of which may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (19) an aromatic ring assembly group which is composed of two or three rings selected from the class consisting of a C_{6-14} aromatic hydrocarbon, a C_{6-14} quinone and a 5- to 14-membered aromatic heterocyclic ring containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms in addition to carbon atoms, are directly bonded to each other via a single bond, and which group may be substituted by 1 to 5

substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, and (20) a fused bi- or tri-cyclic C_{10-14} aryl or 9- to 14-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7- membered saturated cyclic

amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, or

(c) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl, which ring may be further substituted by 1 to 3 substituents selected from the group consisting of oxo, C_{1-6} alkyl and hydroxy, apart from the group of the formula: $-Y-NR^1R^2$ wherein each symbol is as defined above.

3. A compound of claim 1, wherein Ar is an aromatic ring assembly group which may be substituted.

4. A compound of claim 3, wherein the aromatic rings of the aromatic ring assembly group are two or three aromatic rings selected from the group consisting of benzene, thiophene, pyridine, pyrimidine, 1,2,4-oxadiazole, 1,3,4-oxadiazole, naphthalene and

benzofuran.

5. A compound of claim 3, wherein the aromatic ring assembly group is 2-, 3- or 4-biphenylyl.

6. A compound of claim 1, wherein Ar is a 4-biphenylyl which may be substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy.

7. A compound of claim 1, wherein X is a divalent C_{1-6} aliphatic hydrocarbon group which may contain an oxygen atom.

8. A compound of claim 1, wherein X is a C_{1-6} alkylene.

9. A compound of claim 1, wherein X is a group of the formula: $-(CH_2)p-X^1-$ wherein each symbol has the same

meaning as in claim 1.

10. A compound of claim 9, wherein p is 1.

11. A compound of claim 10, wherein X^1 is O.

12. A compound of claim 10, wherein X^1 is NR^{8b} wherein R^{8b} is hydrogen or C_{1-6} alkyl-carbonyl.

13. A compound of claim 1, wherein X^1 is a group of the formula: $-SO_2-NR^8-$ wherein each symbol has the same meaning as in claim 1.

14. A compound of claim 13, wherein R^8 is hydrogen.

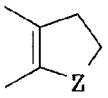
15. A compound of claim 1, wherein Y is a divalent C_{1-6} aliphatic hydrocarbon group.

16. A compound of claim 1, wherein Y is C_{1-6} alkylene.

17. A compound of claim 1, wherein R^1 and R^2 each is C_{1-6} alkyl.

18. A compound of claim 1, wherein Ring A is a benzene ring substituted by the group of the formula: -X-Ar wherein each symbol has the same meaning as in claim 1.

19. A compound of claim 1, wherein Ring B is a 4- to 8-membered ring of the formula:



wherein Z is (i) a bond, (ii) a C_{1-4} alkylene, (iii) a C_{2-4} alkenylene, (iv) $-O-CH_2-$, (v) $-O-CH_2-CH_2-$ or (vi) a group of the formula: $-NR^{8a}-CH_2-$ or $-NR^{8a}-CH_2-CH_2-$ wherein R^{8a} is (a) a hydrogen atom, (b) a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl being optionally condensed with one benzene ring, C_{6-14} aryl or C_{7-19} aralkyl group which may be substituted by 1 to 5 substituents selected form the group consisting of (1) halogen atoms, (2) C_{1-3}

alkylenedioxy, (3) nitro, (4) cyano, (5) optionally halogenated C_{1-6} alkyl, (6) optionally halogenated C_{3-6} cycloalkyl, (7) optionally halogenated C_{1-6} alkoxy, (8) optionally halogenated C_{1-6} alkylthio, (9) hydroxy, (10) amino, (11) mono-C_{1-6} alkylamino, (12) di-C_{1-6} alkylamino, (13) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl, (14) formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido or C_{1-6} alkylsulfonylamino, (15) C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy or nicotinoyloxy, (16) 5- to 7-membered saturated cyclic amino, (17) sulfo, (18) a phenyl or 5- or 6-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, each of which may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6}

alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, (19) an aromatic ring assembly group which is composed of two or three rings selected from the class consisting of a C_{6-14} aromatic hydrocarbon, a C_{6-14} quinone and a 5- to 14-membered aromatic heterocyclic ring containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms in addition to carbon atoms, are directly bonded to each other via a single bond, and which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-

membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, and (20) a fused bi- or tri-cyclic C_{10-14} aryl or 9- to 14-membered aromatic heterocyclic group containing 1 to 4 hetero atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms in addition to carbon atoms, which group may be substituted by 1 to 5 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{3-6} cycloalkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, 5- to 7-membered saturated cyclic amino, formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl, C_{6-10} arylsulfonyl, formylamino, C_{1-6} alkyl-carboxamido, C_{6-10} aryl-carboxamido, C_{1-6} alkoxy-carboxamido, C_{1-6} alkylsulfonylamino, C_{1-6} alkyl-carbonyloxy, C_{6-10} aryl-carbonyloxy, C_{1-6} alkoxy-carbonyloxy, mono-C_{1-6} alkyl-carbamoyloxy, di-C_{1-6} alkyl-carbamoyloxy, C_{6-10} aryl-

carbamoyloxy, nicotinoyloxy and C_{6-10} aryloxy, or

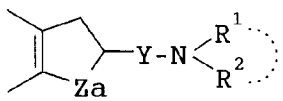
(c) formyl, carboxy, carbamoyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl,

which ring may be further substituted by 1 to 3 substituents selected from the group consisting of oxo, C_{1-6} alkyl and hydroxy, apart from the group of the formula: -Y-NR^1R^2 wherein each symbol has the same meaning as in claim 1.

20. A compound of claim 19, wherein R^{8a} is hydrogen, optionally halogenated C_{1-6} alkyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl.

21. A compound of claim 1, wherein Ring B is a 6-membered carbocyclic or heterocyclic ring substituted by a group of the formula: -Y-NR^1R^2 wherein each symbol has the same meaning as in claim 1.

22. A compound of claim 1, wherein Ring B is a ring of the formula:

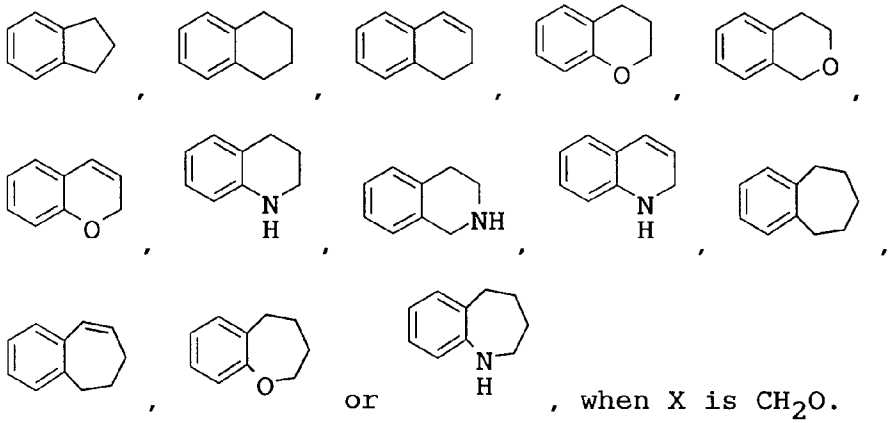


wherein Za is C_{1-3} alkylene or a group of the formula:

$-NR^{8c}-CH_2-$ wherein R^{8c} is hydrogen, optionally halogenated C_{1-6} alkyl, C_{1-6} alkyl-carbonyl, C_{1-6} alkoxy-carbonyl, C_{6-10} aryl-carbonyl, C_{6-10} aryloxy-carbonyl, C_{7-16} aralkyloxy-carbonyl, 5- or 6-membered heterocycle carbonyl, mono-C_{1-6} alkyl-carbamoyl, di-C_{1-6} alkyl-carbamoyl, C_{6-10} aryl-carbamoyl, 5- or 6-membered heterocycle carbamoyl, C_{1-6} alkylsulfonyl or C_{6-10} arylsulfonyl.

23. A compound of claim 22, wherein Za is ethylene.

24. A compound of claim 1, wherein the fused ring to be formed by Ring A and Ring B is a ring of the formula:



, when X is CH_2O.

25. A compound of claim 1, wherein

Ar is 2-, 3- or 4-biphenylyl which may be substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, formyl and C_{1-6} alkyl-carboxamido;

X is C_{1-3} alkylene which may contain an oxygen

atom;

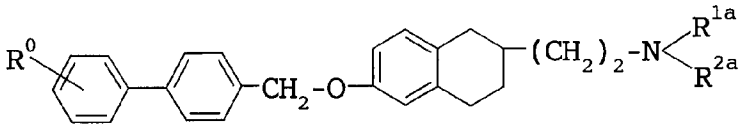
Y is C_{1-6} alkylene;

R^1 and R^2 each is C_{1-6} alkyl;

Ring A is a benzene ring substituted by the group of the formula: -X-Ar wherein each symbol has the same meaning as in claim 1; and

Ring B is a 6-membered carbocyclic or heterocyclic ring substituted by the group of the formula: $-Y-NR^1R^2$ wherein each symbol has the same meaning as in claim 1.

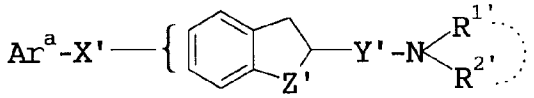
26. A compound of claim 1, which is a compound of the formula:



wherein R^0 is 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl, optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino, formyl and C_{1-6} alkyl-carboxamido; and

R^{1a} and R^{2a} each is C_{1-6} alkyl, or a salt thereof.

27. A compound of claim 1, which is a compound of the formula:



wherein Ar^a is (i) 2, 3- or 4-biphenylyl which may be substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-3} alkylenedioxy, nitro, cyano, optionally halogenated C_{1-6} alkyl,

optionally halogenated C_{1-6} alkoxy, optionally halogenated C_{1-6} alkylthio, amino, formyl and C_{1-6} alkyl-carboxamido, (ii) 4-(2-thienyl)phenyl or 4-(3-thienyl)phenyl, (iii) 4-(3-pyridyl)phenyl, (iv) 6-phenyl-3-pyridyl which may be substituted by a C_{1-6} alkoxy, (v) 5-phenyl-1,3,4-oxadiazol-2-yl, (vi) 4-(2-naphthyl)phenyl, (vii) 4-(2-benzofuranyl)phenyl, (viii) 1- or 2-naphthyl, (ix) 2-quinolyl, (x) 2-benzothiazolyl or (xi) 2-benzofuranyl;

X' is $-CH_2-O-$, $-SO_2-NH-$ or a group of the formula: $-CH_2-NR^{8'}-$ wherein $R^{8'}$ is hydrogen or C_{1-3} alkyl-carbonyl;

Y' is C_{1-6} alkylene;

Z' is $-CH_2-CH_2-$ or a group of the formula: $-NR^{8''}-CH_2-$ wherein $R^{8''}$ is hydrogen, C_{1-3} alkyl, C_{1-3} alkyl-carbonyl or C_{1-3} alkylsulfonyl; and

$R^{1'}$ and $R^{2'}$ each is C_{1-6} alkyl which may be substituted by 1 to 5 substituents selected from the group consisting of di-C_{1-3} alkylamino, C_{1-3} alkoxy-carbonyl and phenyl, or

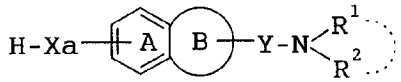
$R^{1'}$ and $R^{2'}$ form, taken together with the adjacent nitrogen atom, a pyrrolidin-1-yl, piperidino or piperazin-1-yl which may be substituted by 1 to 3 substituents selected from the group consisting of hydroxy, C_{1-3} alkoxy-carbonyl, piperidino, phenyl and benzyl, or a salt thereof.

28. A compound of claim 1 which is 6-(4-biphenylyl)methoxy-2-[2-(N,N-dimethylamino)ethyl]tetralin,
6-(4-biphenylyl)methoxy-2-(N,N-dimethylamino)methyltetralin,
2-(N,N-dimethylamino)methyl-6-(4'-methoxybiphenyl-4-

yl)methoxytetralin,
(+)-6-(4-biphenylyl)methoxy-2-[2-(N,N-dimethylamino)ethyl]tetralin,
(+)-6-(4-biphenylyl)methoxy-2-[2-(N,N-diethylamino)ethyl]tetralin,
(+)-2-[2-(N,N-dimethylamino)ethyl]-6-(4'-methylbiphenyl-4-yl)methoxytetralin,
(+)-2-[2-(N,N-dimethylamino)ethyl]-6-(4'-methoxybiphenyl-4-yl)methoxytetralin,
(+)-6-(2',4'-dimethoxybiphenyl-4-yl)methoxy-2-[2-(N,N-dimethylamino)ethyl]tetralin,
(+)-6-[4-(1,3-benzodioxol-5-yl)phenyl]methoxy-2-[2-(N,N-dimethylamino)ethyl]tetralin, or
(+)-6-(3',4'-dimethoxybiphenyl-4-yl)methoxy-2-[2-(N,N-dimethylamino)ethyl]tetralin, or a salt thereof.

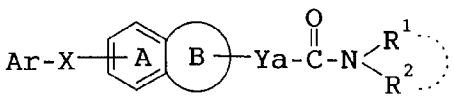
29. A process for producing of a compound of claim 1, which comprises;

i) subjecting a compound of the formula:



wherein Xa represents an oxygen atom, a sulfur atom which may be oxidized or a group of the formula: NR^8 wherein R^8 represents a hydrogen atom, a hydrocarbon group which may be substituted or an acyl; and the other symbols have the same meanings as in claim 1, or a salt thereof, to alkylation or acylation and optionally followed by aryl-coupling of the resultant compound;

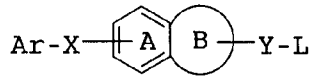
ii) subjecting a compound of the formula:



wherein Ya represents a group to be formed by removing a methylene from Y; and the other symbols have the same meanings as in claim 1, or a salt thereof, to

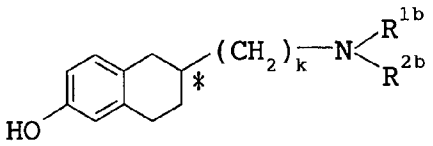
reduction; or

iii) subjecting a compound of the formula:



wherein L represents a leaving group; and the other symbols have the same meanings as in claim 1, to amination.

30. An optical isomer of the compound of the formula:



wherein R^{1b} and R^{2b} each represents methyl or ethyl, k represents 1 or 2, and * indicates the position of the asymmetric carbon, or a salt thereof.

31. A pharmaceutical composition which comprises a compound of claim 1.

32. A pharmaceutical composition of claim 31 which is an inhibitor for production and/or secretion of amyloid-β protein.

33. A pharmaceutical composition of claim 31 which is for preventing and/or treating neurodegenerative diseases caused by amyloid-β protein.

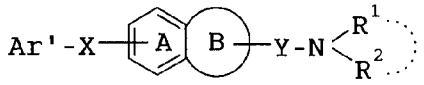
34. A pharmaceutical composition of claim 32, wherein the neurodegenerative disease caused by amyloid-β protein is Alzheimer's disease.

35. A method of inhibiting production and/or secretion of amyloid-β protein in mammal, which comprises administering to said mammal an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable excipient, carrier or diluent.

36. Use of a compound of claim 1 or a salt thereof for manufacturing a pharmaceutical composition for

inhibiting production and/or secretion of amyloid-β protein.

37. An inhibitor for production and/or secretion of amyloid-β protein, which comprises a compound of the formula:



wherein Ar' represents an aromatic group which may be substituted;

X represents (i) a bond, (ii) -S-, -SO- or $-SO_2-$, (iii) a C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene group, each of which may be substituted by 1 to 3 substituents selected from the group consisting of oxo and C_{1-6} alkyl, (iv) -CO-O- or (v) a group of the formula: $-(CH_2)p-X^1-$, $-(CH_2)p-X^1-(CH_2)q-$, $-(CH_2)r-CO-X^1-$, $-SO_2-NR^8-$ or $-(CH_2)r-SO_2-NR^8-$

wherein X^1 represents O or NR^8,

R^8 represents a hydrogen atom, a hydrocarbon group which may be substituted or an acyl, p represents an integer of 0 to 5, q represents an integer of 1 to 5, p+q is an integer of 1 to 5, and r represents an integer of 1 to 4;

Y represents a divalent C_{1-6} aliphatic hydrocarbon group which may contain an oxygen atom or a sulfur atom and may be substituted;

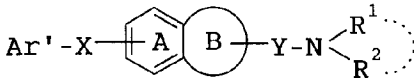
R^1 and R^2 each represents a hydrogen atom or a lower alkyl which may be substituted, or

R^1 and R^2 form, taken together with the adjacent nitrogen atom, a nitrogen-containing heterocyclic ring which may be substituted;

Ring A represents a benzene ring which may be further substituted apart from the group of the formula: -X-Ar

wherein each symbol is as defined above; and
Ring B represents a 4- to 8-membered ring which may be further substituted apart from the group of the formula: $-Y-NR^1R^2$ wherein each symbol is as defined above,
or a salt thereof.

38. A method of inhibiting production and/or secretion of amyloid-β protein in mammal, which comprises administering to said mammal an effective amount of a compound of the formula:



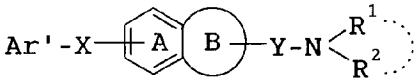
wherein Ar' represents an aromatic group which may be substituted;
X represents (i) a bond, (ii) -S-, -SO- or $-SO_2-$, (iii) a C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene group, each of which may be substituted by 1 to 3 substituents selected from the group consisting of oxo and C_{1-6} alkyl, (iv) -CO-O- or (v) a group of the formula: $-(CH_2)p-X^1-$, $-(CH_2)p-X^1-(CH_2)q-$, $-(CH_2)r-CO-X^1-$, $-SO_2-NR^8-$ or $-(CH_2)r-SO_2-NR^8-$
wherein X^1 represents O or NR^8,
R^8 represents a hydrogen atom, a hydrocarbon group which may be substituted or an acyl, p represents an integer of 0 to 5, q represents an integer of 1 to 5, p+q is an integer of 1 to 5, and r represents an integer of 1 to 4;
Y represents a divalent C_{1-6} aliphatic hydrocarbon group which may contain an oxygen atom or a sulfur atom and may be substituted;
R^1 and R^2 each represents a hydrogen atom or a lower alkyl which may be substituted, or

R^1 and R^2 form, taken together with the adjacent nitrogen atom, a nitrogen-containing heterocyclic ring which may be substituted;

Ring A represents a benzene ring which may be further substituted apart from the group of the formula: -X-Ar wherein each symbol is as defined above; and

Ring B represents a 4- to 8-membered ring which may be further substituted apart from the group of the formula: $-Y-NR^1R^2$ wherein each symbol is as defined above, or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable excipient, carrier or diluent.

39. Use of a compound of the formula:



wherein Ar' represents an aromatic group which may be substituted;

X represents (i) a bond, (ii) -S-, -SO- or $-SO_2-$, (iii) a C_{1-6} alkylene, C_{2-6} alkenylene or C_{2-6} alkynylene group, each of which may be substituted by 1 to 3 substituents selected from the group consisting of oxo and C_{1-6} alkyl, (iv) -CO-O- or (v) a group of the formula: $-(CH_2)p-X^1-$, $-(CH_2)p-X^1-(CH_2)q-$, $-(CH_2)r-CO-X^1-$, $-SO_2-NR^8-$ or $-(CH_2)r-SO_2-NR^8-$

wherein X^1 represents O or NR^8,

R^8 represents a hydrogen atom, a hydrocarbon group which may be substituted or an acyl, p represents an integer of 0 to 5, q represents an integer of 1 to 5, p+q is an integer of 1 to 5, and r represents an integer of 1 to 4;

Y represents a divalent C_{1-6} aliphatic hydrocarbon group which may contain an oxygen atom or a sulfur atom

and may be substituted;

R^1 and R^2 each represents a hydrogen atom or a lower alkyl which may be substituted, or

R^1 and R^2 form, taken together with the adjacent nitrogen atom, a nitrogen-containing heterocyclic ring which may be substituted;

Ring A represents a benzene ring which may be further substituted apart from the group of the formula: -X-Ar wherein each symbol is as defined above; and

Ring B represents a 4- to 8-membered ring which may be further substituted apart from the group of the formula: $-Y-NR^1R^2$ wherein each symbol is as defined above, or a salt thereof for manufacturing a pharmaceutical composition for inhibiting production and/or secretion of amyloid-β protein.

INTERNATIONAL SEARCH REPORT

Inter onal Application No
PCT/JP 98/00780

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07C217/74 A61K31/135 C07C255/54 C07D295/08 C07C233/43
C07D211/26 C07C311/21 C07C211/60 C07C323/19 C07D333/16
C07D213/30 C07D211/44 C07C217/76 C07C233/25 C07D317/54

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 754 455 A (CONSEJO SUPERIOR INVESTIGACION ;UNIV BARCELONA AUTONOMA (ES)) 22 January 1997 cited in the application see claims	1-39
X	EP 0 332 064 A (THOMAE GMBH DR K) 13 September 1989 see claims	1,3,9, 11, 15-25,31
A	WO 95 32967 A (SMITHKLINE BEECHAM PLC ;HAM PETER (GB); GASTER LARAMIE MARY (GB);) 7 December 1995 cited in the application	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 June 1998	12.06.98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pauwels, G

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inte. .onal Application No
PCT/JP 98/00780

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D307/80 C07D211/60 C07C229/14 C07D215/14 C07D271/10
C07D277/64 C07D215/20 C07D215/00 C07D215/58 C07D213/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 June 1998	12.06.98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pauwels, G

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 98/00780

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Although claims 35 and 38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

The scope of the claims is so broad that a complete search appears impossible. For determining the scope of the International Search due account has been taken of Rule 33.3. PCT; special emphasis was put on the subject-matter as illustrated by the examples.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter ional Application No
PCT/JP 98/00780

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0754455 A	22-01-1997	ES 2098186 A	16-04-1997
		CA 2187460 A	15-08-1996
		WO 9624349 A	15-08-1996
EP 0332064 A	13-09-1989	DE 3807813 A	21-09-1989
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		EP 0763034 A	19-03-1997
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		ZA 9504330 A	17-05-1996